

### **REMARKS/ARGUMENTS**

Claims 28-51, 53-58 and 82-120 were pending and presented for examination. Claims 28, 42, 43, 48 and 50 are amended. After entry of these amendments, claims 28-51, 53-58 and 82-120 will be pending.

Claims 28-51, 53-58 and 82-120 stand rejected for alleged obviousness-type non-statutory obviousness-type double patenting over claims 1 to 9 of U.S. Patent No. 6,165,779.

Claims 28-51, 53-58 and 82-120 stand provisionally rejected pursuant to the judicially created obviousness-type nonstatutory double patenting doctrine over claims 1 to 75 of co-pending application no. 10/861,545.

Claims 42-51 and 53-57 stand rejected as allegedly unpatentable in view of an alleged admission in the specification concerning Big Chap on page 12 of the specification.

#### **Support for the Amendments to the Claims**

Claims 28 and 42 and 43 were amended to set forth new formulae. Support for the formulae is found in the specification at Figures 21 and 35 and in the specification at page 12, lines 14 to 22. Support for the salts subject matter is found in the specification at page 12, line 18.

Claim 48 was amended to set forth  $X_3$  is a disaccharide group. Support for this subject matter is found in the previous version of claim 29 and in the specification which sets forth disaccharide groups at page 11, line 24 as well as original claim 30.

Claim 50 was amended to correct its reference to an antecedent.

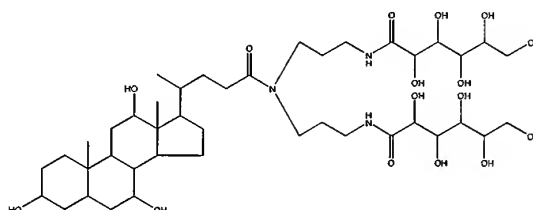
Accordingly, the Applicants believe the amendments to the claims add no new matter and respectfully request their entry.

#### **Response to the rejection of claims 28-51, 53-58 and 82-120 for alleged non-statutory double patenting of the obviousness-type over claims 1 to 9 of U.S. Patent No. 6,165,779.**

This rejection is improperly based upon the unsupported assertion that "Since a person having ordinary skill in the art at the time the claimed invention was made would not have expected the minor changes to affect the property of compounds present in Big CHAP, the

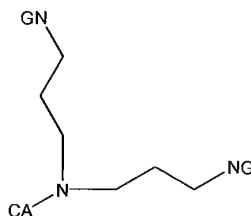
claimed compositions are *prima facie* obvious over the patented compositions. Pursuant to MPEP §2144.03, it is *never* appropriate for an Examiner to rely solely on alleged common knowledge in the art without evidentiary support in the record, as the principal evidence upon which a rejection is based (quoting Zurko, 59 USPQ2d at 1697).

Deeming the changes in structure to be minor does not make them so. BigCHAP is N,N-Bis(3-D-gluconamidopropyl)cholamide and has the following chemical structure:

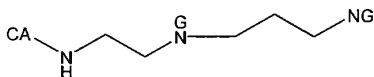


As depicted above, BigCHAP has a chemical formula wherein the cholic acid functional group is attached to the core structure via an amide bond and wherein the nitrogen of the amide bond is *disubstituted*. The formulae of the present invention in contrast sets forth compounds with a different backbone structure wherein  $X_1$  is a cholic acid group or deoxycholic acid group that is attached to the core structure via an amide bond that is *monosubstituted*. As BigCHAP has two saccharide groups, the compound subject matter of the rejected claims is arguably closest, when  $X_2$  and  $X_3$  of the Applicants formula are each a saccharide group. However, even then, the compounds of the claims still substantially differ.

BigCHAP can be represented by the formula:



in which CA is a cholic acid and NG/GN is gluconamido. In contrast, the compound subject matter of claim 28 is arguably closest when both X<sub>2</sub> and X<sub>3</sub> are saccharide moieties which each form a gluconamido moiety with the N to which they are attached and m is 2 and n is 3. In that case, the compound set forth in Claim 28 has the same number of gluconamido groups as BigCHAP and reduces to the formula:

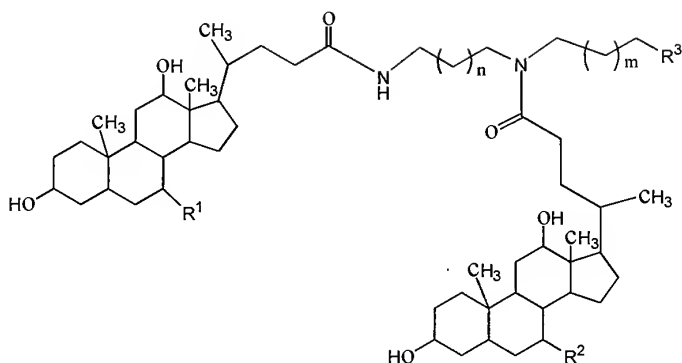


Such a wholesale redesign of the backbone is not fairly represented as being a minor change in structure unassociated with any substantial change in activity. Such an assertion is contrary to the facts with respect to both structure and function. Indeed, the specification teaches that the modifications matter greatly. BigCHAP itself is much less active than its own impurities which share the same backbone as BigCHAP (see Ex. 11, starting at page 32, and particular subsection 6 of Ex. 11 and Figure 20, and Figs. 22 to 24) and is far less active than Applicant's SYN3 as evidenced by several Examples (e.g., Example 14, page 39).

Accordingly, in view of the above, the Applicants respectfully request that this grounds for rejection be reconsidered and withdrawn.

**Response to the provisional rejection of claims 28-51, 53-58 and 82-120 pursuant to the judicially created doctrine of obviousness-type double patenting over claims 1 to 75 of co-pending application no. 10/861,545.**

Recent amendments in the '545 application and in the instant application limit the claims of each to subject matter which does not overlap. In particular, each of the base claims of the '545 patent have been amended to set forth delivery enhancing agents/compounds of the formula:



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Accordingly, the Applicants believe this grounds of rejection has been overcome by request reconsideration and withdrawal of this grounds of rejection.

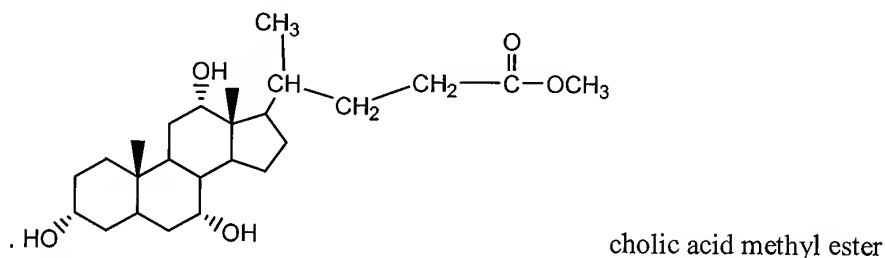
The Office Action alleges that these claims are unpatentable on the grounds that the Applicants admit on page 12 of the specification that the claimed delivery enhancing agents are analogous of impurities found in the commercial product Big CHAP. The pertinent portion of the specification at page 12 recites:

In view of the above recital, the Office Action alleges that:

A person having ordinary skill in the art at the time the claimed invention was made would have been motivated to prepare analogues of known compounds because said person would have expected the resulting compounds to possess similar properties.

Applicants next respectfully traverse the above analysis and conclusion on several grounds.

The four contaminants disclosed to be present in a CalBiochem BigChap preparation are disclosed in Figures 22 to 24 of the specification. The first impurity (Impurity 1 of Figure 22) is a cholic acid methyl ester which is not embraced by the Applicants' claims:



The second impurity (*see*, Impurity 2 of Figure 23) shares the same backbone structure as BigCHAP and is *not* embraced by the compound subject matter of the claims.

Impurity 3, as described in Figure 24, comprises two compounds which also have the backbone structure of BigCHAP. In the first compound (on the left side of the figure), the cholic acid moiety is itself directly substituted with a cholic acid moiety and there are two separate saccharide groups attached to the central N atom. In the second compound (on the right of the figure) there is a first and second saccharide group attached to the central N atom and one of the saccharide groups further has a cholic acid group attached directly to it. Accordingly, the compounds differ according to their backbone structure and, additionally in the presence of either an extra saccharide moiety or an extra cholic acid moiety. *None* of the impurities set forth in Figures 22 to 24 are embraced by the delivery enhancing agent formulae set forth in the amended claims. Here, accordingly, inherency is not a concern, as the compound subject matter of the base claims does not even embrace the disclosed impurities.

Deeming Applicants' discoveries as an "admission" does not place knowledge of those discoveries in the prior art. As a matter of accepted law, obviousness cannot be predicated upon knowledge not found in the prior art. See, MPEP §2141.02 which sets forth that

"Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established." In re Rijckaert, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993). "" None of the structures of these impurities nor any disclosure of their delivery enhancing properties is found in the prior art cited by the Examiner. The Examiner is further respectfully reminded that MPEP §2143, Basic Requirements of a *Prima Facie* case of Obviousness, states that "the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not in Applicant's disclosure. In re Vaeck 20 USPQ2d 1438 (Fed. Cir. 1991)." (see, MPEP §2143 at page 2100-126, last full paragraph, August 2006 revision of MPEP Eight Edition).

Accordingly, the Applicants respectfully request that the above rejection be reconsidered and withdrawn.

**U.S. Patent No. 6,392,069** (already of record)

This patent has issued with claims drawn to compounds embraced by certain of the Applicants' compound claims. Accordingly, once the instant application is deemed to be in condition for an allowance, the Applicants will provide a suitable terminal disclaimer to overcome any double-patenting rejection which may lie over the '069 patent.

**U.S. Patent No. 7,002,027** (already of record)

The above patent issued with claims drawn to compounds which differ from the compounds of the Applicants compound claims in that the patented claims set forth saccharide groups which are monosaccharides whereas the instantly amended compound claims have a saccharide group having from 2 to 8 saccharide groups. The compound subject matter of certain of Applicants' composition claims do embrace certain of the compounds claimed in the '027 patent. Accordingly, once the instant application is deemed to be in condition for an allowance, the Applicants will provide a suitable terminal disclaimer to overcome any double-patenting rejection which may lie over the '027 patent.

**U.S. Applications Nos. 10/455,215 and 10/861,654** (already of record)

The above co-pending applications share some priority benefit with the instant application. The '215 application presents some similar compound and/or composition claims which in a number of instances embrace some common subject matter with the instant claims. The '215 and '654 applications also present related methods claims. The '215 application also presents kit claims.

In view of their respective filing dates, Applicants believe in the event that the instant application is first deemed to be in condition for an allowance, it would be appropriate to withdraw any provisional double patenting rejection that may exist over these co-pending applications. (*see*, MPEP §1490 (V)(D)) and allow the instant application to issue. Any provisional rejections in the co-pending cases can then be made non-provisional.

**U.S. Patent Application No. 10/329043** (already of record)

The above co-pending application presents composition claims directed to lyophilized compositions of Syn3 (the compound of instant claim 98). In view of their respective filing dates, Applicants believe in the event that the instant application is first deemed to be in condition for an allowance, it would be appropriate to withdraw any provisional double patenting rejection that may lie over the '215 application. (*see*, MPEP §1490 (V)(D)).

Appl. No. 10/055,863  
Amdt. dated July 23, 2007  
Reply to Office Action of April 23, 2007

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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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